What research questions should the next generation of birth cohort studies address? An international Delphi study of experts

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Abbreviations: Birth Cohort Studies (BCS); High Income Countries (HIC); Low- Middle-Income Countries (LMIC); Interquartile Range (IQR).

Abstract

Objective: Birth cohort studies (BCS) have generated a wealth of invaluable basic scientific and policy-relevant information on a wide range of issues in child health and development. This study sought to explore what research questions are currently a priority for the next generation of BCS using a 3-round Delphi survey of interdisciplinary experts.

Methods: Twenty-four (Round I, N = 17; Round II, N = 21; Round III, N = 18) experts across a wide range of fields (e.g., psychology, public health and maternal/child health) agreed to participate. In Round I, the expert panel was invited to freely respond to the question, "What are the key scientific questions future birth cohort studies should address?". Content analysis of answers was used to identify 47 questions for rating on perceived importance by the panel in Round II and consensus-achieving questions were identified. Questions that did not reach consensus in Round II were posed again for expert re-rating in Round III.

Results: Twenty six of 47 questions reached consensus in Round II, with an additional 6 reaching consensus in Round III. Consensus-achieving questions rated highly on importance spanned a number of topics, including environmental effects on child development, intergenerational transmission of disadvantage and designing BCS to inform intervention strategies.

Conclusion: Investigating the effects of family/environmental factors and social disadvantage on a child's development should be prioritised in designing future BCS. The panel also recommended that future BCS are designed to inform intervention strategies.

Key Words: Birth cohort studies; Delphi method; consensus; research priorities

What's New: A Delphi method was used to gain consensus on the research priorities of upcoming birth cohort studies. The expert panel prioritized future cohorts to incorporate

interventions and further investigate the effects of societal disadvantage and family/environmental factors on child development.

There is substantial interest in identifying the causal factors that influence early- and later-life health and developmental outcomes. Birth cohort studies (BCS) – longitudinal studies of child development beginning at birth or in utero - are one method particularly suited to this goal.[1,2] A particular advantage of BCS over later-beginning pediatric cohort studies is that they can illuminate the role of pre- and very early post-natal factors[3] and BCS beginning in the prenatal period are additionally valuable for understanding birth outcomes such as prematurity and low gestational weight and their longer-term sequalae. BCS have a strong track record of contributing to policy change;[4] with their findings providing robust evidence that can be utilized by policy-makers and to inform intervention strategies.[5]

BCS do, however, have disadvantages. They are expensive, logistically challenging, time-sensitive, reliant on consistent long-term funding, and slower to produce results than cross-sectional research designs, even when using accelerated cohort designs.[6,7] Moreover, their observational nature means that it is challenging to infer causality.

Given the substantial investment involved in establishing and maintaining a BCS, it is critical that BCS are answering the most pressing research questions in child health and development and as knowledge advances, that they continue to be designed to reflect the most current questions. There is also increasing emphasis on documenting a priori research questions to help guard against flexibility of reporting.[8,9,10] Considering this, there have been calls for BCS to be conducted with clearly justified hypotheses and pre-set research questions.[10,11] Further, by adopting a hypothesis-driven approach, future BCS can focus on the most important scientific questions, leading to a more efficient use of the significant resources required for a successful BCS.[12]

Given the number and diversity of fields that utilize BCS, identifying a manageable number of core research questions that BCS should prioritise is a major challenge; however,

the Delphi method is specifically designed to help achieve consensus among a set of stakeholders with a wide variety of backgrounds and views. It involves an iterative process in which consensus on a particular research question is sought among a panel.[13] and has previously proven useful in identifying future research priorities.[14] Unlike other methods of group interaction (e.g., focus groups), experts in Delphi studies typically participate remotely and anonymously allowing experts to respond freely without being influenced by dominant individuals or conformity bias.[15]

A decade ago, Lawlor and colleagues stated, "…if you asked 10 different researchers what the most important themes were to include in a new birth cohort, you would get 10 different lists."[11] However, to date, no Delphi study has been conducted to address this issue. The aim of the current study was to therefore identify the key scientific questions that the next generation of BCS should address using a Delphi survey of experts.

Method

Sample

Purposive sampling was used to identify suitable candidates for the expert panel. Evidence for Better Lives (EBLS) consortium members were consulted and invited to suggest individuals they believed would be suitable for participation. The EBLS consortium is a group of 15 academics from the UK and low- and middle- income countries (LMIC) who form the leadership of on an eight-site BCS with sites in Jamaica, Vietnam, Ghana, Romania, Philippines, Sri Lanka, South Africa, and Pakistan. A major theme of EBLS is the mitigation of the impacts of early exposure to adversity, such as violence. The consortium members are profiled at: https://www.vrc.crim.cam.ac.uk/vrcresearch/EBLS/ebls-consortium. All share an interest in early child development but are otherwise diverse in terms of their disciplinary background with psychology, paediatrics, public health, child protection, epidemiology,

longitudinal studies, and criminology among the major disciplines represented in the consortium. Each consortium member was consulted via email and invited to suggest an unlimited number of experts based on their knowledge of key experts in BCS. Anyone directly connected to EBLS (e.g., members of the advisory board or other close collaborators) were deemed ineligible to avoid biasing results in favour of the research interests of the EBLS study.

Suggested experts were from fields related to child development, including child protection; pregnancy, neonatology and paediatrics; maternal and child health; psychology; and public health. These fields were chosen in order to recruit an expert panel that was representative of the most prevalent areas of research that conduct and utilize the findings from BCS. Agreement on these fields was achieved prior to participant recruitment by all of the EBLS consortium members; however, the list was considered only indicative and experts from other fields were considered eligible. The main criterion was they were an expert in an area that draws heavily on BCS. Efforts were made to include experts from both high-income countries (HIC) and low- and middle-income countries (LMIC) as the latter are currently considerably under-represented in BCS.[16] Seventy experts were identified as being eligible for participation. Most were senior academics who would by reputation, publication and project leadership track record be considered leaders in their field.

Procedure

Ethics

Ethical approval was obtained from the lead researcher's Psychology Research Ethics Committee (PREC; 270-1819/1). All participants provided informed consent prior to participating.

Delphi Method and Analysis

The Delphi procedure is a standardised method in which a panel answers open question(s) and then rates and re-rates the generated statements to achieve consensus. Experts were invited to provide anonymous answer(s) to the open-ended question, "what are the key scientific questions future birth cohort studies should address?". No specific definition for 'scientific importance' was provided, in order to allow the experts to form their own interpretation and to avoid participants being influenced by the researchers' own notions of scientific importance. As such, elements such as innovation, timeliness, practical importance, creativity, feasibility and other considerations were allowed to be implicitly differentially weighted by the experts in their responses so diversity in responses was not overly constrained. Participants were asked to provide up to three answers. As recommended,[17] three rounds of survey distribution were conducted, using the *Qualtrics* online survey tool.

In Round I (statement generation), experts (N = 70) were sent an invitation e-mail, outlining the study. Experts were informed they would receive no incentives for participating. Thirty-five experts did not respond and 11 declined to participate due to lack of time and/or sufficient expertise. Twenty-four experts were thus provided with a link to Round I in which they were asked to respond to the Delphi's research question. Posed research questions were content analysed in the qualitative coding software, Nvivo. Each research question was coded for references to key words (e.g., "development", "intervention" and "environment") and then grouped into themes by the primary researcher. Quality of the content analysis and the themes generated were reviewed by the study's supervisor. The analysis produced 47 unique statements for rating in Round II.

In Round II (statement rating), all experts were re-invited to rate the statements generated in Round I for scientific importance on a 7-point Likert scale, from 1 = 'not at all important' to 7 = 'very important'. As there is currently no agreement on the optimal number of Likert response categories used in a Delphi,[18] a 7-point scale was selected for use this

number has been found to confer reliable scores and with good discriminant validity.[19] Both the means and interquartile ranges (IQR; i.e., the range between the 25th and 75th percentiles) of the questions' importance scores were calculated using SPSS version 24. IQRs are typically used in Delphi methodologies as their magnitudes are a good indicator of score variation.[20] Questions were considered to have reached consensus when IQRs were <1.00.[20] Questions were then grouped by their level of consensus and perceived importance. Using a method adapted from Dewar and colleagues,[21] the following four categories were used:

1. 'Consensus Achieved': Statement(s) rated "very", "moderately" or "slightly" important by >85% of the experts and an IQR of <1.00.
2. 'Discarded': Statement(s) rated as "very", "moderately" or "slightly" unimportant by >85% of the experts and an IQR of <1.00.
3. 'Unknown': Statement(s) rated as "unsure" by >15% of the experts (i.e., >85% of the experts neither agreed nor disagreed) and an IQR >1.00.
4. 'Discordant': Statement(s) that did not reach consensus across the experts and an IQR >1.00.

For Round III (statement re-rating round), statements categorised as 'Discordant' or 'Unknown' were re-rated by the experts. Participants were informed of the statements that reached consensus in Round II, the group average scores for the discordant questions and their previous rating for each discordant statement in order to encourage experts to move towards a consensus, by reconsidering their previous rating in light of the group averages. All data were collected from April to June of 2019. An overview of the process is shown in Figure 1.

(Insert Figure 1)

Results

Panel Members

Panel sizes of 15 to 30 are considered optimal for Delphi surveys[14] and the current study recruited between 17 and 21 (Round I [N = 17]; Round II [N = 21]; Round III [N = 18]) experts from the 24 who initially expressed interest. Table 1 provides a detailed overview of the samples across the three rounds (see Table 1) and indicates demographic and research profile diversity. For example, 17 experts (8 males; mean age= 59.12, SD = 9.92; 15 senior academics and 2 clinicians) from ten countries (both HIC and LMIC) completed Round I. A large proportion of the participating experts had experience of working and conducting research in LMICs (e.g., Round I; N = 15).

(insert Table 1)

Round I

Round I generated 47 unique scientific questions, which were organised into the following categories; i) 'Environmental Factors' (N = 10; e.g., psychosocial, socioeconomic and geographic effects), ii) 'Informing Interventions' (N = 10; e.g., interventions targeting adversity), iii) 'Biological Factors' (N = 9; e.g., epigenetics and brain alterations), iv) 'Child Development' (N = 8; e.g., external effects on the child's developmental milestones), v) 'Parental Factors' (N = 7; e.g., parental health and behaviours) and vi) 'Nutritional and Health Factors' (N = 3; e.g., healthy behaviours). Four questions were removed as they were considered to be duplicates. Results from Round I post hoc analyses can be seen in section 1.1 of the supplemental materials.

Round II

Of the 17 experts who took part in Round I, 15 continued their participation into Round II and an additional six experts who originally agreed to participate, but did not complete Round I joined the study, giving N = 21. Twenty-six statements reached consensus,

with >85% of the expert panel endorsing the same direction of importance (see Table 2). Questions rated highest in importance (i.e., with an average score of >6.00, or "Moderately Important") contained themes of the transmission of disadvantage, resilience to adversity, the role of biological factors (e.g., epigenetics) in the effects of adversity, and factors that promote healthy behaviours. Eighteen statements were classified as "Discordant", with a further 4 as "Unknown". These statements were retained to be re-rated in Round III. None were classified as "Discarded". Results from Round II post hoc analyses can be seen in section 1.2 of the supplemental materials.

(Table 2)

Round III

Experts who participated in Round II (N = 21) were invited to re-rate the 22 retained "Unknown" and "Discordant". Eighteen experts took part. Experts were reminded of their previous rating in Round II and the overall group average score for each question. Results are shown in Table 3.

(Table 3)

Six additional questions reached consensus, from the categories "Biological Factors" (N = 4) and 'Informing Interventions' (N = 2). A summary of findings across the three rounds is shown in Table 4. Results from Round III post hoc analyses can be seen in section 1.3 of the supplemental materials. Additionally, question-specific and non-specific expert feedback, collected across Rounds I to III, can be seen in supplemental tables S1 and S2.

(Table 4)

Discussion

To the best of our knowledge, this is the first Delphi study to identify key research priorities for the next generation of BCS, using opinions from an interdisciplinary expert panel. Consensus-achieving questions that were rated as high priority spanned several topics, including: the role of the child's family; social adversity; identifying targets for intervention strategies; and the intergenerational transmission of disadvantage.

Most of the consensus-achieving and high-rated questions have already a long history of being investigated in BCS. The question ranked of highest importance was, *"How do environmental and family contexts shape children's developmental outcomes over time?"* Although this question has long been investigated by previous BCS [22] and continues to be explored, [23] the panel likely prioritised it because there are many aspects of family and environmental influences that remain poorly understood or under-researched. As one example, despite increasing awareness of the importance of paternal influences on child development,[24] only a minority of past BCS have collected data from the child's father and with relatively poor response rates.[25] Likewise, data from other family members (e.g., grandparents) who influence on child development have been collected in previous cohort studies only rarely.[26] Considering this, the next generation of BCS could benefit from collecting data from fathers/male caregivers and extended family members, to capture a more complete picture of the family environment.

Identifying the factors that contribute to social inequality and intergenerational transmission of disadvantage was also rated highly on importance by the expert panel. While these issues have also been extensively explored in past BCS,[27,28,29,30] the panel expressed the view that further work is necessary. One issue is that the majority of previous BCS have been conducted in single HICs. [31, 32] As social inequality, its determinants and consequences vary substantially across societies and in particular, at the country level, [33, 34] multi-country BCS may be especially important in illuminating social inequality and its role in child health and

development. Investigating how structural factors interplay with community, family and individual characteristics that cause health and social problems would be particularly beneficial. However, from a practical perspective, co-ordinating BCS a sufficient number of sufficiently diverse countries in order to provide the necessary variation in society-level structural factors is challenging and has been successfully achieved by only a handful of studies thus far.

Many of the experts agreed that the next generation of BCS should have relevance to intervention strategies. Future BCS should thus aim to either incorporate intervention trials[35] or be otherwise designed to inform interventions. For example, the Born in Bradford's Better Start (BiBBS) cohort is one of the first experimental BCS to incorporate multiple intervention strategies that aim to improve early child development.[36] Examples of these interventions include providing community antenatal (e.g., education programmes for vulnerable parents), postnatal (e.g., psychological care for new mothers at risk of mental health difficulties) and early-life support (e.g., screening for language delay in toddlers) to participating families. While BiBBS is still ongoing, results to date have been argued to have improved the evidence-bases for the included interventions, as well as offering important information on effective approaches to improve child health and development to policy makers.[36]

There are a number of potential advantages of embedding interventions in BCS from a trial's perspective; notably, the ability to obtain considerably longer follow-up data on the effects of interventions than in a typical trial.[37] However, there may be disadvantages from the perspective of a BCS. As well as adding significant logistical challenges and costs to an already resource-intensive design,[38] it has been suggested that interventions may undermine the observational nature of these studies.[39] BCS researchers may therefore seek to find alternative paths to informing interventions, such as ensuring that relevant stakeholders, academics, intervention developers and health economists are represented within their teams.

Considering the methodological implications of the top-rated research questions more broadly, arguably all suggested questions could feasibly be addressed without the need for substantial innovation with respect to BCS design. That is, the statistical power, budget, length, measurements, and frequency of follow-up implied (where possible to estimate) were not generally unrealistic. However, each question would potentially have quite different implications for study design. As mentioned above, for example, the question on family contexts implies a need to move beyond gathering data only from mothers; the questions relating to social inequality are best tackled using multiple site BCS that provide variation in social inequality and its structural predictors and questions relating to interventions potentially imply a 'trials within cohort design'.[37] In addition, many of the high scoring research questions that ranked just beyond the top five referred to biological processes which imply a need to collect biosamples from participants. Fortunately, this is becoming increasingly feasible and affordable through methodologies such as dried blood spots and hair samples that can be collected relatively non-invasively, and easily stored, shipped and analysed to provide biomarkers for a range of, genetic and epigenetic, metabolic, environmental exposure, and hormonal factors.[40,41] However, combining the various design features discussed above in a single BCS would be a challenge and it is likely that BCS would prefer to invest in implementing a subset of these design features with a high degree of fidelity.

Finally, it was a key goal of the current study to ensure representation of the views of experts with experience working in LMICs. Approximately 86% of the world's children live in LMIC, where they are likely to be exposed to higher levels of adversity compared to children in HIC.[42] By including experts with experience of conducting research in LMICs, their views can contribute to shaping the research agendas for the next generation of BCS and help address the under-representation of an LMICs perspective.

Strengths and Limitations

The Delphi was conducted online, giving the panel the opportunity to anonymously express their views, free from influences such as groupthink and group polarisation that often occur in other expertise elicitation methods, such as focus groups.[20] An important characteristic of the Delphi procedure,[17] is the provision of individualised feedback at to participants at each round. As both individual and group average scores were fed-back to the panel members, this allowed experts to reappraise their previous ratings for each discordant research question. Our results suggest that this successfully encouraged the panel to move towards consensus as several additional questions reached consensus after this feedback. Finally, assessing consensus quantitatively allows for every expert's opinion to be incorporated into the final results.[43]

There are some limitations to consider. First, the vast majority of the posed questions rated by the expert panel were deemed to be important and the average score range was small (~4 to ~6). This likely reflected the fact that the initial expert panel was effective in generating research questions that would be considered by most other experts to be important. However, it meant that it was difficult to identify only a small number of research questions as definitively of higher priority than others. For this reason, it would be worthwhile to consider how future BCS can address not only the top-rated research questions identified in the current study, but also those that were ranked lower. In addition, the question posed to the panel in Round I, was intentionally left relatively open. While this allowed the experts to respond regardless of their specific expertise and minimised the risk of our instructions biasing responses, the initial panel generated questions of differing levels of specificity. Broader questions may have scored higher by virtue of implicitly incorporating a wider range of sub-questions. Biases may have also arisen during the Delphi procedure. While care was taken to ensure a variety of perspectives were obtained from the participating experts,

academic psychologists represented a large proportion of the panel. However, responses from the panel in Round I spanned a wide variety of topics and were therefore not limited to psychology-based research questions. Similarly, some of the experts were recruited via personal associations with EBLS consortium members, risking the recruitment of those with similar research views. Finally, it is important to note our Delphi survey provides information on priorities that are shared amongst multiple diverse research fields and as such are likely to be less effective at highlighting innovative and/or highly pressing but field-specific priority research questions. Both kinds of research questions are important to consider when designing BCS. Similarly, while we surveyed academics, the views of stakeholders such as policy experts, experts by experience and others who can speak to the practical importance of findings should also be considered when designing BCS. The feasibility and budget implications of the research questions must be considered and weighed against the potential scientific benefits of their incorporation into BCS.

Conclusion

Our study is the first Delphi to identify the key questions that future BCS should address, using the opinion of experts from both HIC and LMIC. It is hoped the findings from this study will be utilized by researchers to help develop *a priori* research questions and hypotheses when designing new BCS; and new waves and sub-studies of existing BCS. The expert panel prioritised research questions that, while having been previously investigated in BCS, remain important and incompletely understood. Identifying the roles of family/environmental factors and social disadvantage in a child's development were deemed of particular importance. Furthermore, BCS should be designed to inform the development of intervention strategies.

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Table 1. Overview of demographics of experts participating in each of the Delphi rounds.				
Sample Characteristic		**Round I (N = 17)**	**Round II (N = 21)**	**Round III (N = 18)**
Sex	Male	8 *(47)*	8 *(38)*	8 *(44)*
	Female	9 *(53)*	13 (*62)*	10 *(56)*
	<35	0 *(0)*	1 *(5)*	1 *(6)*
Age	35-44	1 *(6)*	1 *(5)*	1 *(6)*
	45-54	5 *(29)*	5 *(24)*	5 *(28)*
	55-64	4 *(24)*	7 *(33)*	5 *(28)*
	>65	7 *(41)*	7 *(33)*	6 *(33)*
Ethnicity	Caucasian	13 *(77)*	18 *(86)*	15 *(83)*
	Asian	2 *(12)*	2 *(10)*	2 *(11)*
	Latino	1 *(6)*	1 *(5)*	1 *(6)*
	Afro-European	1 *(6)*	0 *(0)*	0 *(0)*
Country of Origin	UK	5 *(29)*	7 *(33)*	7 *(39)*
	USA	3 *(18)*	4 *(19)*	2 *(11)*
	South Africa	2 *(12)*	3 *(14)*	2 *(11)*
	Other[a]	7 (*41)*	7 *(33)*	7 *(29)*
Country of Origin Income Level[b]	HIC	10 *(59)*	13 *(62)*	10 *(56)*
	LMIC	7 *(41)*	8 *(38)*	8 *(44)*
Area of Expertise	Child Protection	1 *(6)*	1 *(5)*	1 *(6)*
	Pregnancy; Neonatology and/or Paediatrics	1 *(6)*	0 *(0)*	0 *(0)*
	Maternal and Child Health	3 *(18)*	4 *(19)*	3 *(17)*
	Psychology	6 *(35)*	9 *(43)*	8 *(44)*
	Public Health	3 *(18)*	5 *(24)*	4 *(22)*
	Other[c]	3 *(18)*	2 *(10)*	2 *(11)*
Experience working in LMIC[b]	Yes	15 *(88)*	16 *(76)*	16 *(89)*
	No	2 *(12)*	5 *(24)*	2 *(11)*

[a] Other countries of origin were as follows: Iran (N = 1), Brazil (N = 2), Vietnam (N = 1), Peru (N = 1), Italy (N = 1) and Austria (N = 1).
[b] Countries were identified as HIC and LMIC by the World Bank.
[c] Other areas of expertise were as follows: Psychiatry (N = 1), Early Child Education (N = 1) and Childhood Interventions (N = 1).

Table 2. Round II's Consensus-achieving posed scientific questions, ranked on perceived importance.						
Rank	**Posed Scientific Question**	**Mean**	**Agreement (%)**	**SD**	**Range**	**IQR[a]**
Environmental Factors						
1	**How do environmental and family contexts shape children's developmental outcomes over time?**	6.76	100	.539	2	0
2	**How does disadvantage get transmitted from one generation to the next, and how can this be changed?**	6.71	100	.561	2	1
3	**What are the most effective ways to ensure equal opportunities in early life?**	6.24	91	1.09	4	1
4	**How do inequalities in human, social and economic capital play out in the early years of children's lives?**	6.14	86	1.31	4	1
5	**In what ways does the broader social ecology shape child outcomes over time?**	6.10	91	1.04	3	1
6	What are the role of life events (change opportunities) in changing outcomes across the life course?	5.76	91	.995	4	1
7	What are the impacts of psychosocial, sociodemographic and socioeconomic stressors on a newborn/child/adult development; and can these be identified, delineated and quantified?	5.71	86	.956	3	1
Informing Interventions						
1	**What are the leverageable risk and protective factors that can be the target of interventions?**	6.57	100	.676	2	1
2	**What sequence of interventions at which developmental ages can support children's developmental outcomes?**	6.43	95	.926	3	1
3	What would be the effect of interventions to increase fathers' involvement in children's lives?	5.95	91	1.02	3	2
4	What factors contribute towards the development of tolerance and fairness in children? Can these be replicated via interventions?	5.90	91	1.22	4	2
5	What is the long-term impact of participating in different types of programs during the first five years of life (preschool) on later educational achievement?	5.86	95	1.01	4	2
6	What would be the effect of interventions to reduce violence against women on children's health, growth and development?	5.81	91	1.16	4	2
Biological Factors						

1	**What are the biological mechanisms through which adversity affects life-time trajectories?**	6.19	95	.981	3	1
2	**What is the mediating role and reversibility of epigenetic effects on developmental processes and outcomes?**	6.14	91	.910	3	1
Nutritional and Health Factors						
1	**What factors contribute to healthy choices/behaviours over the time course?**	6.10	95	.831	3	1
2	**In settings of high levels of under-nutrition/poverty, how does maternal mental health interact with biological exposures, social adversity, child mental health and factors promoting resilience to affect child development and educational performance up to adolescence?**	6.05	91	1.16	4	1
Parental Factors						
1	What are the interactions between parent's bio-psycho-social development, genetic effects and epigenetic effects on children's bio-psycho-social development?	5.86	91	.930	3	2
2	What are current parenting and family interaction practices and habits and how to they promote or hinder later development?	5.81	95	.814	3	1
3	What are the pre-pregnancy maternal and paternal determinants of life-course outcomes, beginning at the child's birth?	5.57	86	1.12	4	2
4	What drives parental behaviour and what effect does it have on child development?	5.48	86	1.40	5	2
5	What factors in early life influence adult outcomes including productivity, physical health and mental health?	5.32	95	1.08	4	2
Child Development Factors						
1	What factors can help children with mental/physical delays to catch up with normally developed children?	5.86	86	1.19	4	2
2	What is the effect of the environment (communities/schools) on child development?	5.81	91	1.17	4	2
3	How do social determinants and maternal toxic stress exposure influence child birth and development?	5.48	86	1.33	5	2

[a] IQR; Interquartile Range. Posed questions in bold font indicate questions with the highest ranking of importance

Table 3. Results of Round III.

Rank	Posed Scientific Question	Consensus?	Agreement (%)	Round II Average	Round III Average	IQR[a]
Biological Factors						
1	How do genes and environment produce psychopathology?	Yes	100	5.68	5.78	1
2	To what extent are early-life differences genetic, and to what extent are they driven by environment?	Yes	89	5.55	5.39	1
3	Are brain alterations an important factor in underlying how genes and environment produce psychopathology?	Yes	89	5.73	5.67	1
4	Are peripheral alterations (e.g., in the immune system) an important factor in understanding how genes and environment produce psychopathology?	Yes	89	5.41	5.50	1
5	What are the ethical, feasible and reliable ways in which clinical endpoints and stress bio-markers can be incorporated to understand how "stress gets under the skin?"	No	83	5.55	5.50	1
6	Using gene sequencing, should cohorts collect genetic information to allow better separation of nature and nurture?	No	83	5.09	5.33	1
7	How can biological samples be used as a toxic stress exposure measure? (e.g., cortisol, DNA methylation, etc.)	No	83	5.23	5.28	1
Informing Interventions						
1	How can birth cohorts reliably measure key constructs in individuals of different ages?	Yes	94	5.64	5.94	1
2	How can researchers/governments motivate parents to engage in interventions for parenting?	Yes	89	5.00	5.61	1
3	How can interventions target violence against women during pregnancy?	No	78	5.23	5.28	2
4	What would be the effect of interventions on moral values in children's lives?	No	61	5.14	4.83	1
Child Development Factors						
1	How are children in different family forms developing?	No	83	5.05	5.33	1
2	What is the association between early child development and later outcomes in the same areas?	No	83	5.59	5.39	1

3	Are there gender differences in the impact of intensive parents support during pregnancy and early childhood on long term child developmental through epigenetic and brain development?	No	72	5.00	4.94	2
4	What are the main dynamics features of the process of child development and what are the relevant dimensions?	No	72	5.14	5.33	2
5	What is the impact of adverse birth conditions in child development?	No	67	4.95	5.22	3
Environmental Factors						
1	What is the role of socio-emotional factors in positive and negative factors across the life course, starting from birth?	No	72	5.18	5.44	3
2	How can, and are, parents and others in the meso- and exo-system of children's lives (e.g., health services and systems, education and care services and systems) equipping them to cope with the massive changes and disruptions which will accompany climate change?	No	72	5.27	5.11	2
3	Is there a strategy of building community support that can form a redundant supportive network that can facilitate children's development?	No	44	4.91	4.94	3
Parental Factors						
1	How do parents perceive their role in their children's development?	No	56	4.36	4.78	4
2	What are parents' aspirations for their children?	No	50	4.27	4.44	2
Nutritional and Health Factors						
1	What are the nutritional underpinnings for a baby, infant and child to achieve optional growth and neurocognitive development, and not have under or over nutrition?	No	78	5.00	5.39	1

[a] IQR; Interquartile Range.

Table 4. Summary of the Delphi survey findings.

Category	N	Questions Achieving Consensus	Questions not Achieving Consensus	Questions Achieving Consensus (%)	Questions with >6.00 Importance Score
'Informing Interventions'	10	8	2	80	2
'Environmental Factors'	10	7	3	70	5
'Biological Factors'	9	6	3	67	2
'Child Development Factors'	8	3	5	38	0
'Parental Factors'	7	5	2	71	0
'Nutritional Factors'	3	2	1	67	2

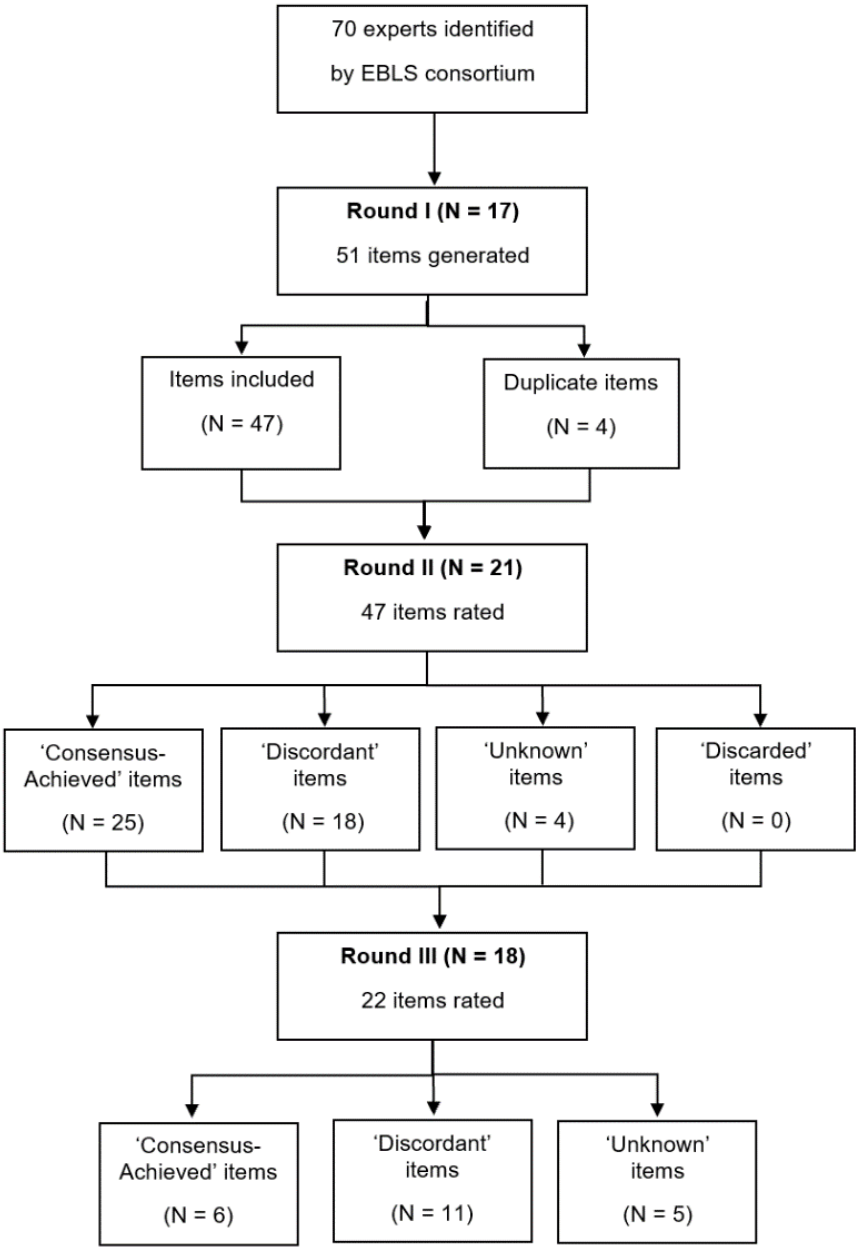

Figure 1. Overview of Delphi procedure.